

Kaplan-Meier curve for individual genotypes against the animal age in months. In case of aggressive metastasis or sarcomas, the animals were euthanized and the tumours were isolated for analysis. Adult *Cpt1c^{gt/gt}* and *wild type* mice were individually housed in calorimeter cages with *ad libitum* access to standard chow and water. During seven dark/light cycles we measured the respiratory exchange ratio, the energy expenditure rate, the food intake and the activity rate.

Results: A higher survival rate and a lower frequency of tumors were observed in the *Nf1^{+/-}:p53^{+/-}:Cpt1c^{gt/gt}* mice if compared with the *Nf1^{+/-}:p53^{+/-}* group. *Nf1^{+/-}:p53^{+/-}:Cpt1c^{gt/gt}* mice were leaner than the *Cpt1c^{gt/gt}*, the *Nf1^{+/-}:p53^{+/-}* and the WT control mice. Interestingly, rather than developing tumors, 28% of the *Nf1^{+/-}:p53^{+/-}:Cpt1c^{gt/gt}* died due to cachexia, muscle fatigue and seizures. According to literature, *Cpt1c^{gt/gt}* mice have a low food intake and this might be the cause of their lower body weight. Our group however, obtained opposite results: *Cpt1c^{gt/gt}* mice have the same food intake and activity rate if compared with WT mice, but have higher energy expenditure (EE). This higher EE rate might be the cause of the lean phenotype.

Conclusions: Our results indicate that *Cpt1c* expression in the *Nf1^{+/-}:p53^{+/-}* mice might contribute to a more malignant phenotype of cancer cells. *Nf1^{+/-}:p53^{+/-}:Cpt1c^{gt/gt}* developed tumors less frequently and had a higher survival rate. However, they showed a cachectic phenotype that still needs to be elucidated. *Cpt1c*-deficient mice have a lower body weight and higher EE rate if compared to WT mice. We hypothesize that tumor cells lacking *Cpt1c* suffer from insufficient nutrient supply which may cause the delay in tumor growth. Understanding how *Cpt1c* expression influences cancer cells might give new insights for the prediction of therapy efficiency and furthermore may lead to novel therapeutic approaches. *Cpt1c* is a potential target for the treatment of hypoxia- and radiation-resistant tumors.

POSTER: CLINICAL TRACK: PAEDIATRICS

PO-0739

Prognostic factors for toxicity in childhood medulloblastoma treated with Helical Tomotherapy

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Purpose/Objective: Medulloblastoma is one of the most common childhood brain malignancies. The purpose of this study is to evaluate the tolerability and prognostic factors for toxicity of craniospinal irradiation (CSI) with helical tomotherapy (HT) in the treatment of medulloblastoma.

Materials and Methods: The institutional review board approved a retrospective chart review, which was conducted for pediatric patients with primary medulloblastoma treated with craniospinal HT from May 2007 through December 2010. Inclusion criteria were having a primary diagnosis of medulloblastoma, no prior history of RT, age < 18 years old, and having a minimum follow up of 6 months for living patients. We found 19 patients (standard risk, N=10; high risk, N=9) who met such criteria. HT regimens to the neuroaxis included: 23.4 Gy at 1.8 Gy/fraction (N=10), 36 Gy at 1.8 Gy/fraction (N=7), and 39 Gy bid at 1.3 Gy/fraction (N=2). The tumor bed received 54-60 Gy at 1.5-1.8 Gy/fraction. Toxicity was scored using the Radiation Therapy Oncology Group scoring system. These groups were divided according to the toxicity location as follows: overall toxicity, cranial toxicity (defined as any non-hematological toxicity experienced above the neck), body toxicity (defined as any non-hematological toxicity experienced below the neck), and hematological toxicity. Spearman's rank correlation coefficient was used to correlate patient, tumor, and dosimetric factors with the grade of acute toxicity or the overall survival time.

Results: The median age at diagnosis was 5 years (range, 2-14) and the median follow-up for living patients (N=14) was 40 months (range, 10-62). Two and three-year overall survival was 75% and 68%, respectively. Only 2 patients had a local failure in the surgical bed. The most common acute toxicity was hematological (79%), being grade 2 and grade 3 in 4 (21%) and 11 (58%) cases, respectively. Specifically, grade 3 acute anemia, neutropenia, and thrombopenia was observed in 5% (N=1), 53% (N=10), and 10% (N=2), respectively. In addition, there were two cases of grade 2 skin toxicity, seven cases of

grade 2 upper gastrointestinal toxicity, and one case of grade 2 pharynx toxicity. There were no cases of grade 4 acute toxicity. No grade ≥2 late toxicities were observed. A longer time between diagnosis and radiation therapy associated with shorter overall survival ($P=0.03$). Older children were associated with higher grades of acute body toxicity ($P=0.004$), whereas longer radiation treatments associated with higher grades of acute hematological toxicity ($P=0.034$).

Conclusions: Although the follow-up is relatively short, clinical outcomes of CSI schedule with HT are favorable, resulting in lower doses to the normal tissue. Acute and late toxicities are tolerable without severe late side effects. Further research is necessary to assess longer late toxicity and tumor control outcomes.

PO-0740

The risk of secondary cancer from radiotherapy planning PET and CT compared to therapy for paediatric cancer patients

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Purpose/Objective: To evaluate the risk of FDG-PET/CT (Positron Emission Tomography/Computed Tomography) scanning of paediatric patients in terms of radiation-induced secondary cancers. The risk of cancer induction was estimated and the resulting reduction of life expectancy was compared to the life years lost (LYL) attributable to the cancer therapy.

Materials and Methods: Forty paediatric cancer patients (≤18 years old) with a FDG-PET/CT-scan performed between 2004 and 2012 were included in the study. The majority of the malignancies were lymphomas and sarcomas. Patient-specific information regarding the PET/CT scans was extracted from clinical records. For seventeen patients, radiotherapy plans (RTPs) were made on CT-data from a different scan and that additional dose was included in the risk estimation for the combined diagnostics. The effective doses (EDs) from the FDG-PET scans were estimated using the conversion factors reported in ICRP 106. The EDs from the CT scans were assessed using a commercially available spreadsheet-based software with Monte Carlo simulated dose data. The risk of solid cancer induction was estimated according to the risk models presented in the BEIR VII report. The risk estimates formed the basis for estimating the lifetime attributable risk (LAR) of developing a solid cancer. The LAR was used with the cancer prognosis to estimate the LYL compared to the general population.

Results: The mean estimated LAR of developing solid cancer due to the diagnostic scans was 0.42% (median: 0.37%, range: 0.12-1.30%) for the whole population. For the female and male groups, the LAR was 0.50% (median: 0.43%, range: 0.29-1.30% and 0.34% (median: 0.33%, range: 0.12-0.75%), respectively.

The effective doses are presented in table 1 and figure 1a.

The LYL attributable to late effects from cancer therapy was estimated to 5.0 years and 3.7 years for females and males, respectively (derived from data in a report on excess mortality on patients in the childhood cancer survivor study). The ratios of attributable LYL for diagnostic scans and cancer therapy were <3%, see figure 1b.

	Mean	Median	Range
Total effective dose Diagnostic scans Females	35.24 mSv	34.3 mSv	13.0-90.1 mSv
Total effective dose Diagnostic scans Males	42.1 mSv	39.1 mSv	12.3-78.1 mSv
% of total effective dose from 18F-FDG-PET Females	25.8%	21.3%	8.6-63.1%
% of total effective dose from 18F-FDG-PET Males	23.1%	21.2%	6.2-63.0%

Table 1: Effective Doses.

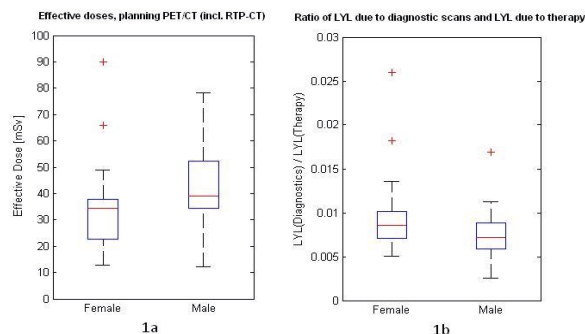


Figure 1: a) Effective doses and b) LYL-ratios.

Conclusions: The LYL attributable to cancer therapy were orders of magnitudes larger than the LYL attributable to the diagnostic scans used for radiotherapy planning. However, the uncertainty in the present estimates of LYL were considerable, and would benefit from more exact risk models.

POSTER: CLINICAL TRACK: PALLIATION/SUPPORTIVE CARE/PATIENT SUPPORT

PO-0741

Neurocognitive status as QoL index in solitary brain metastasis patients treated with WBRT vs SRS after surgery

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Purpose/Objective: Patient-(age, performance status, psychological distress), disease-(type, localization) and treatment (neurosurgery, radiotherapy, chemotherapy)-related factors may impact on cognitive functioning of metastasis patients. Neuropsychological involvement may be an important factor, reducing quality of daily life (QoL). This study aimed to evaluate difference between whole brain radiotherapy (WBRT) and radiosurgery (SRS) on neurocognitive functioning accordingly on QoL of brain metastasis patients. We did a randomized controlled trial to test our prediction.

Materials and Methods: Patients with solitary brain metastasis of solid tumors with stable systemic disease tumors and KPS \geq 70 were treated with complete surgery and randomly assigned to adjuvant WBRT (30 Gy in 10 fractions) or SRS (17-20 Gy single fraction) on surgical cavity (max diameter 3.5 cm). The primary end point was local control, secondary end points survival, quality of life and toxicity. 65 patients, fulfilling the study inclusion criteria, were treated since December 2009 to September 2012. After randomization 42 subjects were assigned to SRS group, 23 to WBRT. All subjects were tested to assess global cognitive functioning using the Mini Mental State Examination (MMSE): at baseline (T1) before radiotherapy treatment, after one year (T2) and after 2 years (T3). Preliminary results were available for 55 subjects at T1, for 25 subjects at T2, for 6 at T3.

Results: The pretreatment MMSE was available for 37 patients randomized for SRS, and 18 for WBRT. The sample did not present cognitive deficit post surgery and no statistically significant difference were found between the baseline MMSE of two groups ($P = 0,064$). Of the 25 patients underwent the follow-up MMSE at one year, 10 (40%) had improved their scores and 5 (20%) worsened in SRS group; all subjects (100%) obtained lower scores in WBRT group. From preliminary evaluations it was found a statistically significant difference between the neurocognitive performance of WBRT group and the SRS one ($P = 0,039$). Currently, there's no sufficient data at 2 years.

Conclusions: The results of this study have revealed that the long-term adverse effect of WBRT on neurocognitive functioning might not be negligible also for the quality of life of brain metastases patients.

PO-0742

Palliative radiotherapy for bone metastases. Differences in the symptomatic relief according to the primary tumor

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Purpose/Objective: Many studies have assessed the fractionation scheme to choose the most appropriate in individual cases. Various fractionation schemes can provide a response equivalent to the control of pain, although longer treatment has the advantage of a lower incidence of reprocessing the same site. The aim of our retrospective study was to evaluate the differences in requirements and the impact of different radiotherapy schedules on patients symptoms in relationship to primary tumor type and quality of life.

Materials and Methods: We analyzed 458 treatments of palliative radiotherapy for bone metastases. For these patients, we did control of pain, performance status and pain-therapy, before treatment, after treatment, and 180 days after the end of treatment. We analyzed the data using the T-test for paired data and the ANOVA test and we performed a comparison of performance status and pain in relation to the type of fractionation.

Results: We noticed an improvement in performance status and pain relief in all groups, but the pain improvement was more evident in patients treated with single fraction, while we noticed a difference of the average KI before and after RT, even if not statistically significant, in favor of the longest fractionation (30 Gy) schemes. We also have focused our attention in patients with primary tumors with expected greater overall survival, in particular, we considered patients treated for bone metastases from breast cancer. The differences between averages with ANOVA test seemed to demonstrate an advantage in favor of the 30Gy schedule for the KI (ns $p = 0.105$), while they were favorable to the single fraction of 8 Gy for the NRS ($p < 0.001$).

Conclusions: We have obtained data which are in line with the statement made in recent years on the equivalence of the various types of fractionation for the control of pain from bone metastases, but that suggest a greater attention to the radiation oncologist in the choice of the patient to be subjected to various types of fractionation. It is recommended to put a considerable amount of attention over which the clinical condition of patients, the primary tumor (breast) of patients who, for the greater life expectancy resulting from the natural history of cancer, should have a better access to a more prolonged treatment.

PO-0743

Once weekly stereotactic radiotherapy for oligometastatic patients: compliance and preliminary efficacy.

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Purpose/Objective: This retrospective analysis reports the outcomes obtained with an original once weekly stereotactic radiotherapy fractionation delivered for patients affected by evolving oligometastases from different solid malignancies.

Materials and Methods: From 2009 to 2011 patients with symptomatic and/or evolving oligometastases were submitted to a median 5-fraction-cycle of stereotactic radiotherapy by delivering only one a fraction per week in order to exploit a radiobiological rationale designed to increase the therapeutic index. Individual fractionation was mainly planned according to patient performance status, oligometastases size and site and record of previous irradiation in the same site.

Results: Thirty-six patients in stage IV UICC-TNM affected by oligometastases were treated with image-guided/intensity modulated stereotactic tomotherapy by delivering a single weekly radiation. Median age was 70 yrs (34-89 yrs). The median weekly single dose, number of fractions and overall total radiation dose were 7 Gy, 5 fractions and 35 Gy, respectively. Thirty-five (97%) patients completed the treatment schedule. No patient suffered mild or severe radiation-related side effects. Twenty-one (87%) out of 24 patients with local pain had complete symptomatic response within 30 days from the end of radiotherapy. Local control assessed at imaging after SRT was evidenced in 30 (83%) of patients. Median time to response after the end of radiotherapy was 40 days.